Anesthetic and Life Support Drugs Advisory Committee
Topics for Discussion

Disease Modifying Agents

Consider, in your discussions, agents that may exert their effect by a mechanism that might slow the course of disease and also agents that might actually reverse the course of disease.

1. **Entry Criteria**

    - Discuss the subject of entry criteria for trials of disease modifying agents for peripheral neuropathy.

    - Include consideration of diagnosis and severity, baseline diabetic control, and methods of optimizing diabetic control prior to and after randomization, for example, the use of a prerandomization baseline stabilization period.

2. **Endpoints**

    - Discuss what you would consider clinically relevant endpoints for trials evaluating the treatment of peripheral neuropathy designed to modify or reverse the course of the disease.

    - Include a discussion of neuropathy-related morbidity, neuropathy scales, electrophysiological testing, quantitative sensory testing, and skin biopsy.

    - Discuss the role of composite endpoints versus single-item endpoints.

    - Discuss the role of quality of life measures in the evaluation of disease-modifying agents.

    - Consider which of the above measures are actually surrogate markers of the desired clinical effect, and whether any positive effects on surrogate endpoints are sufficiently well correlated with clinical effects so as to serve as a basis for approval, with post-approval validation

3. **Duration of Studies**

    - Discuss the duration of trials needed to demonstrate an effect of treatment on peripheral neuropathy with disease modifying agents.

Symptomatic Claims

- Discuss what you would consider clinically relevant endpoints for trials evaluating the treatment of the overall symptoms of peripheral neuropathy.
- Include a discussion of neuropathy-related morbidity, neuropathy scales
- Discuss the role of composite endpoints versus single-item endpoints.
- Discuss the use of quantitative measures of nerve structure and function (eg, electrophysiological testing, quantitative sensory testing, and skin biopsy) as supportive outcome measures.
- Discuss the role of quality of life measures in the evaluation of symptom reduction

Neuropathic Pain

1. **Entry Criteria**

- Consider the subject of entry criteria for trials of drugs used to treat neuropathic pain.
- Include discussion of diagnosis, severity, measures of neuropathic signs and symptoms such as allodynia and hypesthesia, duration of symptoms prior to enrollment, and, in the specific case of painful diabetic neuropathy, quantitative measures of sensory loss such as sural nerve action potential.

2. **Endpoints**

- Discuss what you would consider clinically relevant endpoints for trials evaluating the treatment of neuropathic pain.
- Include in your discussion the role of pain scales, quantitative measures of nerve function, functional scales and quality of life scales.
- Consider whether there is a consensus regarding what would represent a clinically meaningful effect for each of those metrics.

3. **Generalizability of neuropathic pain across etiologies**

- Discuss the degree to which successful treatment of one etiologic type of neuropathic pain can be applied to another etiologic type of neuropathic pain. For example, can successful treatment of painful diabetic neuropathy be

extrapolated to post-herpetic neuralgia, CRPS, cervical radiculopathy, trigeminal neuralgia, and phantom limb pain?

- Should a general claim for neuropathic pain be entertained, and, if so, what should constitute the burden of evidence for that claim?